

WHAT IS CLAIMED IS:

1. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT,
wherein the tumor is a microsatellite instability-high colorectal cancer, a microsatellite stable colorectal cancer, a triple negative breast cancer, a Merkel cell carcinoma, an endometrial cancer, or an esophageal cancer; and
wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
2. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT in combination with a PD-1 antagonist or a PD-L1 antagonist,
wherein the tumor is a microsatellite instability-high colorectal cancer, a microsatellite stable colorectal cancer, a triple negative breast cancer, a Merkel cell carcinoma, an endometrial cancer, or an esophageal cancer, and
wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
3. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT,
wherein the tumor is resistant or refractory to treatment with a PD-1 antagonist or a PD-L1 antagonist; and
wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1

comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).

4. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT in combination with a PD-1 antagonist or a PD-L1 antagonist, wherein the tumor is resistant or refractory to treatment with a PD-1 antagonist or a PD-L1 antagonist as a single agent; and wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
5. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT, wherein the subject has previously been treated with a PD-1 antagonist or a PD-L1 antagonist as a single agent; and wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
6. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT in combination with a PD-1 antagonist or a PD-L1 antagonist, wherein the subject has previously been treated with a PD-1 antagonist or a PD-L1 antagonist as a single agent; and wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1

comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).

7. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT,
wherein the tumor expresses poliovirus receptor (PVR) and/or poliovirus receptor-related 2 (PVRL2); and
wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
8. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT in combination with a PD-1 antagonist or a PD-L1 antagonist,
wherein the tumor expresses poliovirus receptor (PVR) and/or poliovirus receptor-related 2 (PVRL2); and
wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
9. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT,
wherein the tumor comprises tumor-infiltrating lymphocytes (TILs); and
wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1

comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).

10. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT in combination with a PD-1 antagonist or a PD-L1 antagonist, wherein the tumor comprises tumor-infiltrating lymphocytes; and wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
11. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT, wherein the tumor comprises regulatory T-cells; and wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
12. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT in combination with a PD-1 antagonist or a PD-L1 antagonist, wherein the tumor comprises regulatory T-cells; and wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).

13. The method of any one of claims 3-6, wherein there is tumor growth progression during or after treatment with a PD-1 antagonist or a PD-L1 antagonist.
14. The method of any one of claims 3-6, wherein there is tumor growth recurrence after treatment with a PD-1 antagonist or a PD-L1 antagonist.
15. The method of claim 14, wherein the tumor recurrence is local recurrence, regional recurrence, or distant recurrence.
16. The method of claim 3 or claim 4, wherein the tumor is resistant or refractory to treatment with an anti-PD-1 antibody.
17. The method of claim 3 or claim 4, wherein the tumor is resistant or refractory to treatment with an anti-PD-L1 antibody.
18. The method of claim 5 or claim 6, wherein the subject has previously been treated with an anti-PD-1 antibody.
19. The method of claim 5 or claim 6, wherein the subject has previously been treated with an anti-PD-L1 antibody.
20. The method of any one of claims 2, 4, 6, 8, 10, or 12, wherein the combination therapy comprises an anti-PD-1 antibody.
21. The method of any one of claims 2, 4, 6, 8, 10, or 12, wherein the combination therapy comprises an anti-PD-L1 antibody.
22. The method of any one of claims 3-21, wherein the tumor is selected from the group consisting of: lung tumor, liver tumor, breast tumor, renal cell carcinoma/kidney tumor, prostate tumor, gastrointestinal/gastric tumor, melanoma, cervical tumor, bladder tumor, glioblastoma, head and neck tumor, pancreatic tumor, ovarian tumor, colorectal tumor, endometrial tumor, and esophageal tumor.

23. The method of any one of claims 1-22, wherein the antibody that binds human TIGIT comprises a heavy chain variable region comprising SEQ ID NO:10 and a light chain variable region comprising SEQ ID NO:11.
24. The method of any one of claims 1-23, wherein the antibody that binds human TIGIT is a monoclonal antibody.
25. The method of any one of claims 1-24, wherein the antibody that binds human TIGIT is a bispecific antibody.
26. The method of any one of claims 1-25, wherein the antibody that binds human TIGIT is an antibody fragment comprising an antigen binding site.
27. The method of any one of claims 1-25, wherein the antibody that binds human TIGIT is an IgG1 antibody.
28. The method of any one of claims 1-25, wherein the antibody that binds human TIGIT is an IgG4 antibody.
29. The method of any one of claims 1-25, wherein the antibody that binds human TIGIT comprises a heavy chain amino acid sequence of SEQ ID NO:13 and a light chain amino acid sequence of SEQ ID NO:15.
30. The method of any one of claims 1-25, wherein the antibody that binds human TIGIT comprises a heavy chain amino acid sequence of SEQ ID NO:17 and a light chain amino acid sequence of SEQ ID NO:15.
31. The method of any one of claims 1-26, wherein the antibody that binds human TIGIT comprises a heavy chain variable region encoded by the plasmid deposited with ATCC as Designation No. PTA-122346 and a light chain variable region encoded by the plasmid deposited with ATCC as Designation No. PTA-122347.
32. The method of any one of claims 1-31, which increases T effector cells within the tumor and/or the tumor microenvironment.

33. The method of any one of claims 1-31, which increases T effector cell activity within the tumor and/or the tumor microenvironment.
34. The method of any one of claims 1-31, which depletes regulatory T-cells within the tumor and/or the tumor microenvironment.
35. The method of any one of claims 1-31, which inhibits and/or decreases the suppressive activity of Tregs within the tumor and/or the tumor microenvironment.
36. The method of any one of claims 1-35, wherein the antibody that binds human TIGIT is administered once every week, once every two weeks, once every three weeks, or once every four weeks.
37. The method of claim 36, wherein the antibody that binds human TIGIT is administered about once every two weeks or once every three weeks.
38. The method of any one of claims 1-37, wherein the antibody that binds human TIGIT is administered at a dose of about 0.1mg/kg to about 25 mg/kg.
39. The method of claim 38, wherein the antibody that binds human TIGIT is administered at a dose of about 0.3mg/kg, about 1mg/kg, about 3mg/kg, about 10mg/kg, or about 15mg/kg.
40. The method of any one of claims 1-39, which further comprises administering at least one additional therapeutic agent.
41. The method of claim 40, wherein the additional therapeutic agent is a chemotherapeutic agent.
42. The method of claim 40, wherein the additional therapeutic agent is an antibody.
43. The method of claim 40, wherein the additional therapeutic agent is an immunotherapeutic agent.

44. The method of claim 43, wherein the immunotherapeutic agent is selected from the group consisting of: GM-CSF, M-CSF, G-CSF, IL-2, IL-3, IL-12, IL-15, B7-1 (CD80), B7-2 (CD86), 4-1BB ligand, GITRL, OX40L, CD40L, anti-CD3 antibody, anti-CTLA-4 antibody, anti-GITR antibody, anti-OX40 antibody, anti-4-1BB antibody, anti-LAG-3 antibody, and anti-TIM-3 antibody.
45. The method of claim 40, wherein the additional therapeutic agent is an inhibitor of the Notch pathway, the Wnt pathway, or the RSPO/LGR pathway.
46. The method of any one of claims 1-45, wherein the subject has had a tumor or a cancer at least partially removed.
47. A method of inhibiting tumor growth in a subject, comprising administering to the subject a therapeutically effective amount of an antibody that specifically binds the extracellular domain of human TIGIT,
wherein the tumor is a head and neck cancer, esophageal/gastroesophageal cancer, gastric cancer, colorectal cancer, anal cancer, hepatocellular cancer/liver cancer, cervical cancer, lung cancer, melanoma, Merkel cell carcinoma, renal cell carcinoma/kidney cancer, bladder cancer, ovarian cancer, pancreatic cancer, endometrial cancer, and triple negative breast cancer, a known MSI high solid tumor (including MSI CRC) or a MSS colorectal cancer;
wherein the tumor is resistant or refractory to treatment with an anti-PD-1 antibody or an anti-PD-L1 antibody; and
wherein the antibody that binds human TIGIT comprises a heavy chain CDR1 comprising TSDYAWN (SEQ ID NO:4), a heavy chain CDR2 comprising YISYSGSTSYNPSLRS (SEQ ID NO:5), a heavy chain CDR3 comprising ARRQVGLGFAY (SEQ ID NO:6), a light chain CDR1 comprising KASQDVSTAVA (SEQ ID NO:7), a light chain CDR2 comprising SASYRYT (SEQ ID NO:8), and a light chain CDR3 comprising QQHYSTP (SEQ ID NO:9).
48. The method of claim 47, wherein the subject has previously been treated with an anti-PD-1 antibody or an anti-PD-L1 antibody.
49. The method of any one of claims 1-48, wherein the antibody that specifically binds the extracellular domain of human TIGIT is administered to the subject at a dose of about 0.1 mg/kg,

about 0.3 mg/kg, about 1 mg/kg, about 1.5 mg/kg, about 2 mg/kg, about 2.5 mg/kg, about 3 mg/kg, about 5 mg/kg, about 7.5 mg/kg, about 10 mg/kg, or about 15 mg/kg.

50. The method of any one of claims 1-49, wherein the antibody that specifically binds the extracellular domain of human TIGIT is administered once every week, once every two weeks, once every three weeks, or once every four weeks.
51. The method of any one of claims 1-50, wherein the subject has a histologically confirmed advanced relapsed or refractory solid tumor.